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# Early and Late Results of *Ex Vivo* Repair and Autotransplantation in Solitary Kidneys

J. Morin, B. Chavent*, A. Duprey, J.N. Albertini, J.P. Favre, X. Barral

*Cardiovascular Surgery, CHU Saint-Etienne, Avenue Albert Raimond, Saint-Priest en Jarez, France*

**WHAT THIS PAPER ADDS**

- This topic that has never been published before (*ex vivo* repair and autotransplantation in solitary kidney) has shown that renal function is not impaired by peroperative renal artery clamping and renal ischaemia.

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ABSTRACT

*Introduction:* Autotransplantation of a solitary kidney provides an excellent opportunity to study the immediate and long-term consequences of intra-operative renal ischaemia. The purpose of this report is to describe a series of nine patients who underwent *ex vivo* repair and autotransplantation on solitary kidneys.

*Patients and methods:* The series included six females and three males with a mean age of 36 years. Seven of the nine patients were hypertensive (mean number of anti-hypertensive agents: 3). Two patients had chronic renal failure (serum creatinine levels: 192 and 205 μmol $l^{-1}$). All arteries except one with Takayasu disease were affected by dysplastic aneurysm or fibrodysplasia lesion. There was no atherosclerotic lesion. The mean number of renal artery branches repaired was 3.1 per patient. Mean duration of ischaemia was 161 min.

*Results:* Creatinaemia increased in all patients following the procedure. Creatinaemia and clearance returned to preoperative values between the 3rd and 10th postoperative days. One kidney was lost due to renal vein thrombosis. Late findings indicated that renal function was stable and there was no deterioration in the function of the autotransplanted kidneys after a follow-up period of 89 months. Preoperative versus postoperative creatinaemia and clearance levels were respectively 111 vs. 105 μmol $l^{-1}$ and 66.9 vs. 62.0 ml $min^{-1}$ (ns). During the same time, the mean number of anti-hypertensive agents decreased slightly from 3 to 2.5.

*Conclusion:* In this small series of patients who underwent *ex vivo* repair and autotransplantation on solitary kidneys, intra-operative renal ischaemia had no detrimental effect on renal function.



The impact of intra-operative ischaemia on kidney function is difficult to evaluate objectively during renal artery repair. When transplantation is performed using a kidney from a living donor, the early rejection phenomenon and potential deleterious effects of immunosuppression can obscure the effects of ischaemia. Similarly ischaemic effects can be masked by the presence of the contralateral kidney in conventional renal artery repair surgery. Autotransplantation of a solitary kidney provides a much more pertinent model to study the immediate and long-term consequences of ischaemia on renal function and arterial blood pressure. The purpose of this report was to describe the early and late results of intra-operative renal ischaemia in a series of nine patients who underwent autotransplantation after *ex vivo* repair on solitary kidneys.

## Methods

This is a retrospective review of nine patients who underwent autotransplantation between 1994 and 2010. There were six

* Corresponding author.
*E-mail address:* chavent.bertrand@hotmail.fr (B. Chavent).

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females and three males with a mean age of 36 years (range, 12–59 years). Demographic and preoperative data are listed in Table 1.

Autotransplantation after *ex vivo* renal artery branch repair was performed in all cases. Kidneys were explanted without ureteral section. They were protected by selective perfusion using a preservation solution at 4 °C. The protection protocol consisted of administration of a bolus of 1 l of solution followed by reinjection of 200 cc every 20 min. Over the course of the study period, the preservation solution changed from EuroCollins® in the first five patients to Custodiol® in the last four patients. Branch repair was done using a hypogastric arterial graft in six patients and a superficial femoral artery graft in three. The kidneys were autotransplanted to the terminal aorta and vena cava for right kidneys and on common iliac vessels for the left ones.

All procedures were performed using a cell-saver device so that exogenous blood transfusion was not required in any case.

The primary study 'end' point was recovery of renal function assessed based on daily in-hospital monitoring and outpatient follow-up. Renal function was estimated by calculating creatinaemia clearance using the Cockcroft formula.

Secondary 'end' points were patency of revascularised arteries and arterial blood pressure assessed directly from blood pressure measurements and indirectly from the number of anti-hypertensive agents prescribed during follow-up.

Considering the small number of patients, we used a Wilcoxon test to determine differences in pre- and postoperative renal function using Statistical Package for Social Sciences (SPSS) software (version 11.6.1). A $p$-value $< 0.05$ was considered to indicate statistical significance.

## Results

### *Early outcome*

The mean number of renal artery branches repaired was 3.1 per patient. The mean duration of ischaemia was 161 min. Completion angiography was performed in all patients and demonstrated no significant defect (Fig. 1 (A)–(C)). Kidney loss due to venous thrombosis occurred in one patient, who was treated 3 months later by cadaveric donor transplantation. Another patient required re-operation for treatment of iliac artery occlusion (Table 2).

Renal function during the in-hospital postoperative period is shown in Fig. 2. Values were available for only eight patients, that is, excluding the kidney-loss patient.

All patients exhibited an increase in postoperative creatinaemia during the first postoperative days. In all but two patients, peak values were reached between the 2nd and 4th day and ranged from 95 to 200 μmol $l^{-1}$. The two patients with higher peak ranges, that is, 205–663 μmol $l^{-1}$ in one and 192–285 μmol $l^{-1}$ in the other, presented preoperative renal insufficiency. Creatinaemia values returned to preoperative levels between the 3rd and 10th day. Analysis of creatinine values showed no significant differences between preoperative and discharge values in any patient, including the two patients who presented with renal insufficiency preoperatively.

The mean renal clearance increased between the pre- and postoperative period. This improvement was not significant ($p > 0.05$) and was not found in all kidneys. Indeed, the clearance of two kidneys decreased after surgery. The mean ischaemia duration for those two kidneys was 115 and 175 min, respectively.

Concerning renal function, there were no significant differences in clearance ($p = 0.31$) and creatininaemia ($p = 0.78$) between the pre- and postoperative period.

Analysis of preoperative and postoperative renal function as a function of the duration of renal ischaemia is shown in Table 3. Preoperative and immediate postoperative blood pressure and anti-hypertensive treatment data are summarised in Table 4. Preoperative and discharge mean arterial blood pressures were not significantly different in any patient.

At the time of discharge, patency of the revascularised artery branches was checked by CT-angiography in six patients, renal scintigraphy in four, arteriography in two and colour duplex ultrasound in one. One patient suffered renal vein thrombosis with kidney loss in the immediate postoperative period. Thrombosis was observed in 3 of the 27 reconstructed renal arteries branches. The primary patency rate was 89%.

### *Late outcome*

The mean duration of follow-up was 89.4 ± 67.2 months (Table 4). No patient was lost to follow-up. All the patients were contacted for a clinical and morphological control with colour duplex ultrasound when data were collected.

### *Renal function*

Long-term creatinaemia values and mean creatinaemia clearance values were stable: 111 vs. 105 μmol $l^{-1}$ and 66.9 vs. 62.0 ml $min^{-1}$, respectively. No patients required secondary dialysis. The child who required transplantation after early kidney loss due to venous thrombosis had a functional graft at the end of study follow-up (Table 4). In fact, thrombosis of renal artery branches during the postoperative period had no influence on the renal function. It occurred in three arteries in three different patients on the 27 that were repaired, and it also can be explained by the fact that in every case, thrombosis occurred in small branches with diameter ≤2 mm, corresponding to a small territory of kidney.

### *Arterial hypertension*

In the seven patients initially treated for hypertension, mean preoperative blood pressure was 149/84 mmHg. At the end of

**Table 1**
Demographic and preoperative data in study population.

| Patient | Age | Sex | AHT | N° anti-AHT agents | Creat Cl ml/mn | Indication for autotransplantation | Contralateral kidney |
|---|---|---|---|---|---|---|---|
| 1 | 27 | M | NO | 0 | 106 | Aneurysm due to dysplasia – 25.8 mm | Agenesis |
| 2 | 40 | F | YES | 1 | 75 | Aneurysm due to dysplasia – 24 mm | Hypoplasia |
| 3 | 44 | F | YES | 1 | 83 | Aneurysm due to dysplasia – 23 mm | Nephrectomy for aneurysm |
| 4 | 59 | F | YES | 2 | 20 | Aneurysm – 30 mm | Agenesis |
| 5 | 15 | M | YES | 4 | 81 | Takayasu disease | Nephrectomy for ATH |
| 6 | 48 | F | NO | 0 | 71 | Aneurysm – 25 mm | Agenesis |
| 7 | 20 | F | YES | 5 | 35 | Occlusion due to dysplasia | Agenesis |
| 8 | 58 | F | YES | 3 | 52 | Aneurysm – 30 mm | Nephrectomy for nephrolithiasis |
| 9 | 12 | M | YES | 3 | 58 | Dysplasia | Nephrectomy for ATH |

Abbreviations: AHT: arterial hypertension, Creat Cl: creatinemia clearance.

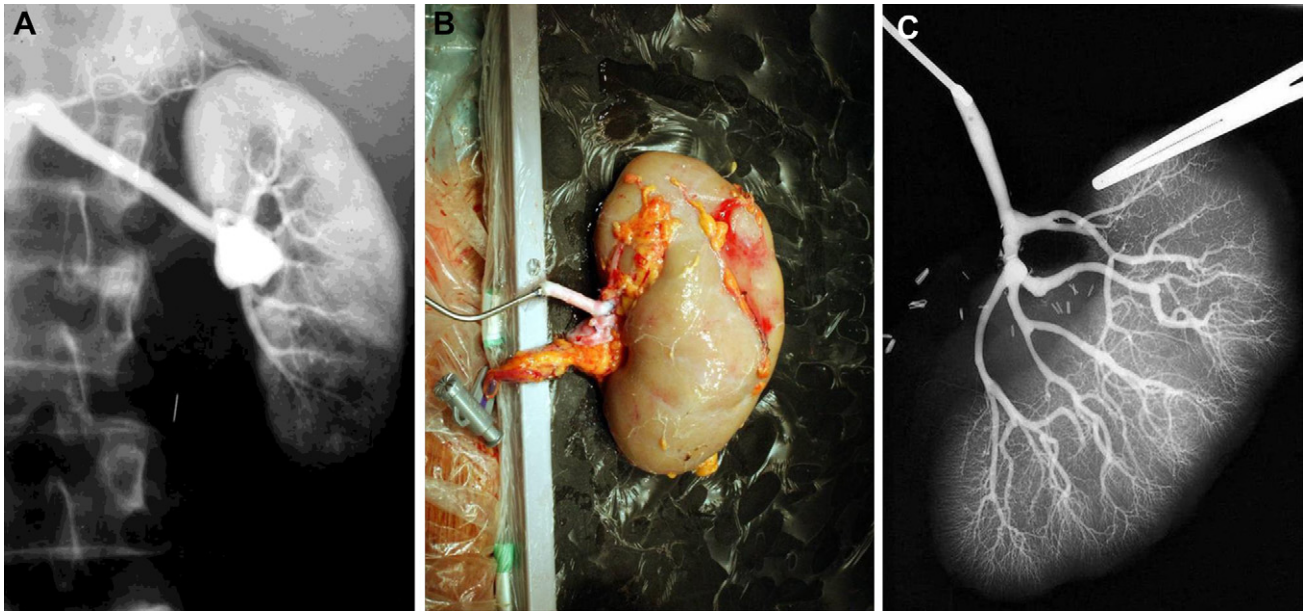


**Figure 1.** (A) Left renal aneurysm in a solitary kidney. (B) same patient after ex-vivo repair. (C) same patient per op angiographic control.

follow-up, mean systolic pressure was 127/72 mmHg. This value corresponds to the mean of individual blood pressure measurements made during outpatient examinations. The mean number of hypertensive agents used decreased slightly from 3.0 to 2.5 per patient. The number of agents decreased or remained unchanged in all but one patient (Table 4).

*Late patency*

No deterioration in kidney function was observed during follow-up and no patient required re-operation or secondary angioplasty.

## Discussion

Autotransplantation in patients with a solitary kidney provided an excellent model to study the direct impact of ischaemia during renal artery repair on renal function.

It is important to note that two of the seven patients whose preoperative renal function was normal presented with renal artery stenosis greater than 80%.[1] Despite high-grade stenosis, creatinine clearances were 81 and 58 ml $min^{-1}$ that can be considered as normal for patients with solitary kidneys. This finding is consistent with the hypothesis that fibro-dysplastic disease has a less detrimental effect on renal function than atherosclerotic vascular disease.[2,3] In patients with renal artery fibrodysplasia, glomerular filtration rate and renal reserve function remain good so that renal function can remain normal despite severe lesions.

Two patients in this series presented with preoperative renal insufficiency. The first had bilateral renal artery occlusion with intrahilar reinjection of the right kidney via the perirenal circle. Renal insufficiency was linked to chronic low renal flow rate. The second patient had a large isolated aneurysm with blockage of the branches of the renal artery resulting in a major decrease in blood flow and thus in glomerular filtration.

Excluding the two patients with preoperative renal insufficiency, the mean time for renal function to return to preoperative levels after artery repair was 4 days (Fig. 1). This short recovery time in comparison with cases involving acute tubular necrosis suggests that parenchymal damage was minimal. In the four patients who underwent scintigraphy for postoperative functional monitoring, recovery was confirmed by observation of normal Mag 3 uptake within 1 week. All patients who did not present renal insufficiency showed a slight increase in clearance measured the evening before the procedure and on the eighth postoperative day: 65 vs. 71 ml $min^{-1}$ (NS, $p = 0.35$). For the two patients who presented with preoperative renal insufficiency, recovery of renal function took longer, that is, between the fifth and tenth postoperative day. Recovery time appears to have been linked to the extent of initial renal insufficiency. Both patients showed a dramatic improvement in flow rate with clearance increasing from 20 to 32 ml $min^{-1}$ in one case and from 35 to 48 ml $min^{-1}$ in the other.

No correlation was found between either clamping duration of the number of arteries repaired. All repairs were performed during hypothermia induced by perfusion of renal preservation solution,

**Table 2**
Early outcomes of autotransplantation in 9 patients with solitary kidneys.

| Patient | N° of renal artery branches repaired | Duration of ischemia (mn) | Duration of hospitalization (days) | Complications |
|---|---|---|---|---|
| 1 | 5 | 220 | 10 | |
| 2 | 4 | 175 | 8 | |
| 3 | 3 | 115 | 20 | Pancreatitis |
| 4 | 2 | 80 | 16 | Acute lower limb ischemia |
| 5 | 2 | 96 | 12 | |
| 6 | 3 | 205 | 8 | |
| 7 | 4 | 262 | 21 | |
| 8 | 4 | 135 | 16 | Pulmonary embolism |
| 9 | 2 | 150 | 51 | Renal Vein thrombosis |

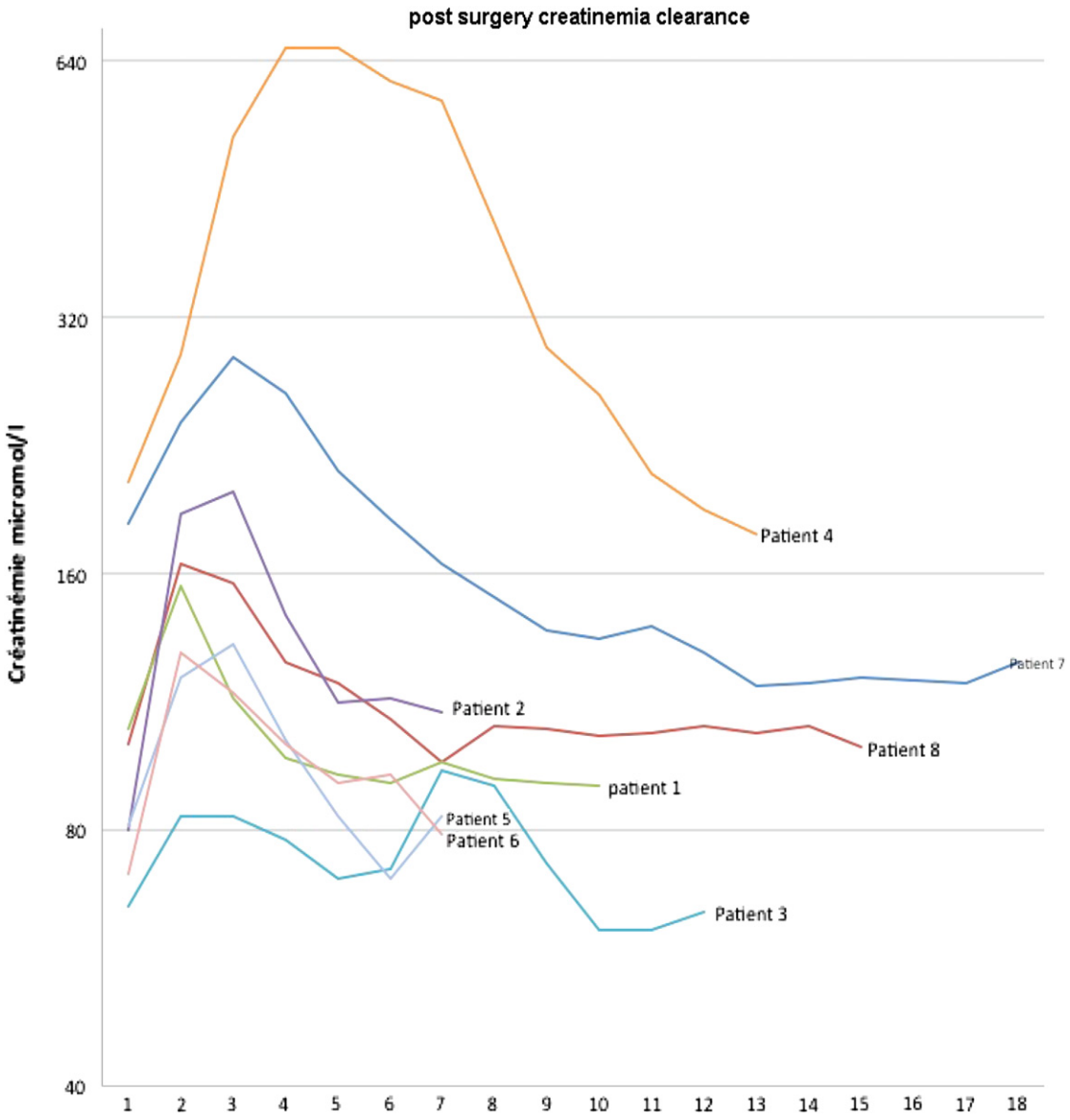


**Figure 2.** Early effect on renal function.

thus allowing prolonged ischaemia, that is, more than 2 h in all cases, without parenchymal damage. In reports describing *in situ* procedures, deleterious effects of renal ischaemia have been observed after ischaemia times ranging from 20 to 90 min[3,4] This is a major advantage of *ex vivo* surgery that allows complex repair procedures that conventional or percutaneous procedures cannot achieve without kidney damage.

The follow-up period in this study was 89 months. Findings indicated that *ex vivo* repair followed by autotransplantation provides durable results with stable renal function.

**Table 3**
Creatinemia clearance after autotransplantation in 9 patients with solitary kidneys.

| Patient | Preoperative clearance (ml/min) | Postoperative clearance (ml/min) | Duration of ischemia (min) | Duration of follow-up (months) |
|---|---|---|---|---|
| 1 | 106 | 124 | 220 | 74 |
| 2 | 75 | 61 | 175 | 7 |
| 3 | 83 | 66 | 115 | 87 |
| 4 | 20 | 32 | 80 | 137 |
| 5 | 81 | 87 | 96 | 41 |
| 6 | 71 | 72 | 205 | 35 |
| 7 | 35 | 42 | 262 | 201 |
| 8 | 52 | 83 | 135 | 48 |
| 9 | 58 | Dialysis | 150 | 175 |

**Table 4**
Arterial blood pressure and anti-hypertensive treatment before and after autotransplantation in 9 patients with solitary kidneys.

| Patient | Pre-op mAP* | Discharge mAP | Pre-op n° of anti-hypertensive agents | N° of post-op anti-AHT | Duration of follow-up (months) |
|---|---|---|---|---|---|
| 1 | 91 | 83 | 0 | 0 | 74 |
| 2 | 100 | 97 | 1 | 1 | 7 |
| 3 | 96 | 90 | 1 | 1 | 87 |
| 4 | 117 | 93 | 4 | 6 | 137 |
| 5 | 137 | 93 | 4 | 1 | 41 |
| 6 | 76 | 83 | 0 | 0 | 35 |
| 7 | 140 | 97 | 5 | 3 | 201 |
| 8 | 76 | 87 | 3 | 3 | 48 |
| 9 | 109 | Dialysis | 3 | 4 | 175 |

*Abbreviation: mAP: mean arterial pressure mmHg.

Thus, this study confirmed excellent long-term outcome for patients treated for non-atherosclerotic arterial disease. This result is consistent with previous reports describing *ex vivo* repair in patients with two kidneys.[5]

Drawing conclusions about the short-term and long-term outcomes of *ex vivo* repair and autotransplantation on blood pressure is difficult in this small series of patients treated for various indications. Of the six patients treated for aneurysm, four presented with AHT and two had normal blood pressure. The remaining two patients presented with renovascular AHT related to high-grade stenosis of the renal artery. Branch repair never led to resolution of AHT, and all six patients with preoperative AHT required hypertensive-drug treatment throughout the 89-month follow-up period. The number of anti-hypertensive drugs used was only slightly modified dropping from 3.0 to 2.5 per patient. In this study, surgical management of aneurysm had no benefit in terms of reducing hypertension. In the four patients with AHT due to aneurysm, no decrease in the number of agents was observed during follow-up. The relationship between aneurysm and renovascular hypertension remains unclear.[6] Conversely, as documented extensively by previous authors, repair was highly effective in the two patients with occlusive disease.[7]

## Conclusion

In this small series of patients who underwent *ex vivo* renal artery repair and autotransplantation on solitary kidneys, intraoperative ischaemia with autotransplantation worsened renal function for a short period, from 4 to 10 days in our experience, without consequences on long-term renal function. Renal function and long-term patency of the revascularised renal arteries were excellent, and management of aneurysm has minimal effect on hypertension.

## Conflict of Interest/Funding

None.

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